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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/663,889	09/18/2000	Gary J. Nabel	8642/91	6450

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EXAMINER	
PARAS JR, PETER	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 01/29/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/663,889	NABEL ET AL.	
	Examiner	Art Unit	
	Peter Paras, Jr.	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 August 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *17 and 19-36* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *17 and 19-36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 8/8/03 has been entered.

The amendment received on 8/8/03 has been entered. Claims 17 and 19-36 have been amended. Claims 1, 18 and 37-54 have been cancelled. Claims 17 and 19-36 are pending and are under current consideration.

Priority

This application repeats a substantial portion of prior Application Nos. 08/533,942, 09/031,572, and 09/426,325, filed 9/26/95, 2/26/98 and 10/25/99, respectively and adds and claims additional disclosure not presented in the prior application; the additional disclosure is **a combination**, which comprises a nucleic acid comprising a gene encoding p21 and a catheter. Since this application names an inventor or inventors named in the prior application, it may constitute a continuation-in-part of the prior application. Should applicant desire to obtain the benefit of the filing date of the prior application, attention is directed to 35 U.S.C. 120 and 37 CFR 1.78.

Applicant's claim of priority to Application Nos. 08/533,942, 09/031,572, and 09/426,325, now US Patent Nos. 5,863,904, 6,057,300, 6,218,372 respectively, is

denied. The parent applications fail to fulfill the requirements of 35 U.S.C 120 by not meeting the requirements of the first paragraph of 35 U.S.C. 112, particularly written description and new matter, necessary to support the claims of the instant application. See the MPEP at 201.11. In particular, the claim limitations as follows are not described in the instant specification: a combination comprising a catheter and a nucleic acid comprising a gene encoding p21. See the rejection under 35 U.S.C. 112, 1st paragraph, below.

Applicants submit that newly added amendments to claims 17 and 19-36 directed to a combination comprising a nucleic acid comprising a gene encoding p21 and a catheter are fully supported by the instant specification and also by parent applications 08/533,942, 09/031,572, and 09/426,325. See pages 6-7 of the amendment.

In response, the Examiner argues the instant application and parent applications do not support a combination comprising a nucleic acid comprising a gene encoding p21 and a catheter. The passages of the applications listed by Applicant at pages 6-7 of the amendment do not provide support for a combination of gene encoding p21 and a catheter. The recited passages describe a method of using a catheter for administration of a vector comprising a p21 gene. However, the recited passages do not describe or suggest a combination of a gene encoding p21 and a catheter as a product. It appears the instant claims are directed to a "product" comprising a gene encoding p21 and a catheter rather than a method requiring the use of separate products including a gene encoding p21 and a catheter. It would appear that applicant is attempting to satisfy the written description requirement of 35 USC 112, first paragraph, through obviousness.

Obviousness, however, cannot be relied upon for satisfaction of the written description requirement. In support of this position, attention is directed to the decision in *University of California v. Eli Lilly and Co.* (Fed. Cir. 1997) 43 USPQ2d at 1405, citing *Lockwood v. American Airlines Inc.* (Fed. Cir. 1997) 41 USPQ2d at 1966: It was held that a description, which renders obvious a claimed invention, is not sufficient to satisfy the written description requirement of that invention. Applicants are reminded that material needed to accord an application a filing date may not be incorporated by reference. Therefore, if a continuation or divisional application as originally filed incorporates by reference material omitted from the application papers, which is needed to accord the application a filing date, the application will not be entitled to a filing date. See MPEP § 201.06(c).

Accordingly, priority stands to the parent applications stands denied.

Oath/Declaration

This application presents a claim for subject matter not originally claimed or embraced in the statement of the invention. The newly claimed subject matter is a kit comprising a catheter and a nucleic acid comprising a gene encoding p21. A supplemental oath or declaration is required under 37 CFR 1.67. The new oath or declaration must properly identify the application of which it is to form a part, preferably by application number and filing date in the body of the oath or declaration. See MPEP §§ 602.01 and 602.02. Also see the MPEP 602.05(a).

Applicants submit the instant amendments to the claims, directed to a combination of a gene comprising a p12 gene and a catheter, are sufficient to overcome the requirement for a new oath/declaration. See page 7 of the amendment.

In response, the Examiner argues the instant presents claims directed to subject matter not originally claimed or embraced in the statement of the invention. As discussed above, it appears support for the newly added claim limitations directed to a combination comprising a nucleic acid comprising a gene encoding p21 and a catheter is lacking in the parent applications.

Accordingly, a new oath/declaration is required.

Claim Rejections - 35 USC § 112, 1st paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 17 and 19-36 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 17 (and dependent claims 19-36) are directed to **a combination comprising a catheter and a nucleic acid comprising a gene encoding p21**.

The specification provides no implicit or explicit support for a combination comprising a catheter and a nucleic acid comprising a gene encoding p21 encompassed by the bolded text. The specification has only provided support for use of a catheter and an expression vector comprising a gene encoding p21 in a treatment method but has not otherwise even contemplated a combination, as a product, comprising the same.

Applicants are reminded that it is their burden to show where the specification supports any amendments to the claims. See 37 CFR 1.121 (b)(2)(iii), the MPEP 714.02, 3rd paragraph, last sentence and also the MPEP 2163.07, last sentence.

MPEP 2163.06 notes "If new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. 112, first paragraph - written description requirement. *In re Rasmussen*, 650 F.2d 1212, 211 USPQ 323 (CCPA 1981)." MPEP 2163.02 teaches that "Whenever the issue arises, the fundamental factual inquiry is whether a claim defines an invention that is clearly conveyed to those skilled in the art at the time the application was filed...If a claim is amended to include subject matter, limitations, or terminology not present in the application as filed, involving a departure from, addition to, or deletion from the disclosure of the application as filed, the examiner should conclude that the claimed subject matter is not described in that application. MPEP 2163.06 further notes "When an amendment is filed in reply to an objection or rejection based on 35 U.S.C. 112, first paragraph, a study of the entire application is often necessary to determine whether or not "new matter" is involved. *Applicant should therefore specifically point out the support for any amendments made to the disclosure.*

Applicants submit that the instant claim amendments directed to a combination comprising a nucleic acid comprising a p21 gene and a catheter are disclosed in the instant application. See page 7 of the amendment.

In response, the Examiner maintains, as discussed above, the newly added claim limitations directed to a combination comprising a nucleic acid comprising a p21 gene and a catheter are not described in the instant application. Therefore the newly added claim limitations constitute new matter.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 17 and 19-36 are rejected under 35 U.S.C. 102(b) as being anticipated by Nabel et al (US 5,863,904).

The claims are directed to a combination comprising a catheter and a nucleic acid comprising a gene encoding p21. For the purposes of this rejection the limitation "combination" is not given patentable weight, as it is an intended use for its components.

Nabel et al teach the administration of an adenoviral vector comprising a gene encoding p21 via a double-balloon catheter to the iliofemoral artery of a pig. See column 6, lines 22-58. Nabel et al also teach that the expression vector may be

combined with a pharmaceutical carrier. See column 4, lines 31-33. Nabel et al further teach that the gene encoding p21 can be inserted into viral vectors, such as adenoviral and retroviral vectors (see column 2 beginning on line 57 and bridging to column 3, line 22), wherein the viral vector may be incorporation into an acceptable formulation provided the viral particles are inactivated (see column 4, lines 37-50). Nabel et al teach that certain viral promoters, such as the CMV and RSV promoters may be inserted into an expression vector to drive expression of the p21 gene. See column 3 at lines 2-4. Nabel et al teach that such an expression vector containing a gene encoding p21 can be incorporated into a liposome and then delivered to a specific tissue. See column 4, lines 25-30. Finally Nabel et al teach that p21 can be expressed as a fusion protein, wherein the gene encoding p21 is fused to a second gene encoding an immunotherapeutic agent, genetic therapeutic agent, cytokine, or a prodrug converting enzyme, particularly thymidine kinase. See column 3 lines 53-60.

Thus, the teachings of Nabel anticipate all of the instant claim limitations.

Applicants submit in view of their arguments with respect to priority the instant application is entitled a priority date of 6/26/95. Therefore Applicants argue the '904 patent is disqualified as prior art over the instant application.

In response, the Examiner argues, as discussed above, that priority to parent applications (08/533,942, 09/031,572, and 09/426,325) is denied. Therefore, the instant application is not entitled a priority date of 6/26/95 and the '904 patent anticipates the instantly claimed invention.

Claims 17, 20-22, and 31 are rejected under 35 U.S.C. 102(b) as being anticipated by Xiong et al (Nature, 1993, 366: 701-704).

The claims are directed to a combination comprising a catheter and a nucleic acid comprising a gene encoding p21.

For the purpose of this rejection the term "catheter" is interpreted broadly such that it reads on tubing, such as a pipette tip or an Eppendorf tube. Xiong et al teach cloning of cDNA encoding p21. Xiong et al further teach isolation of p21 cDNA from a cDNA library prepared from U118 cells and translation *in vitro* of the cDNA to produce the p12 protein. Since Xiong et al describe cloning of p21 cDNA, it is apparent typical laboratory supplies such as pipette tips or eppendorf tubes were used in the cloning/isolation protocol. At any time p21 cDNA was present in tubing such as a pipette tip or an eppendorf tube the claims were anticipated. Furthermore, Xiong et al has taught that the p21 cDNA was translated *in vitro*, which means the p21 cDNA had to have been inserted into an expression vector. Finally, as p21 cDNA was isolated from a cDNA library it is clear any vector comprising the p21 cDNA would have also comprised a second gene, particularly an antibiotic resistance gene, which is typically used as a selection marker in DNA purification protocols.

Thus, the teachings of Xiong et al anticipate all of the instant claim limitations.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 17 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Xiong taken with Nabel et al (Science 1990, 249: 1285-1288).

The claims are directed to a combination comprising a catheter, particularly a double balloon catheter) and a nucleic acid comprising a gene encoding p21.

Xiong et al teach cloning of cDNA encoding p21. See page 701. Xiong et al discuss that p21 inhibits cell proliferation upon overexpression in mammalian cells. See pages 703-704.

Xiong et al do not teach a double-balloon catheter.

However, at the time the instant invention was made, it was known in the art that a double-balloon catheter could be used to deliver heterologous genes directly into arterial walls as evidenced by Nabel et al. Nabel et al teach use of a double-balloon catheter to introduce nucleic acid molecules directly into arterial walls. See pages 1285-1286. On page 1287 Nabel et al suggest that a double-balloon catheter could be used to introduce recombinant genes, which inhibit smooth muscle cell proliferation, directly in the site of angioplasty to inhibit smooth muscle cell proliferation to prevent restenosis.

Accordingly, at the time the claimed invention was made, it would have been obvious for one of ordinary skill in the art to combine a p21 gene and a catheter, particularly a double-balloon catheter. One of ordinary skill in the art would have been sufficiently motivated to combine a p21 gene and a catheter as Xiong et al taught that p21 is an inhibitor of cell proliferation and more particularly because Nabel et al represent that a double-balloon catheter can be used to introduce recombinant genes, which inhibit smooth muscle cell proliferation, directly in the site of angioplasty to inhibit smooth muscle cell proliferation to prevent restenosis (see page 1287).

Thus, the claimed invention, as a whole, is clearly *prima facie* obvious in the absence of evidence to the contrary.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner(s) should be directed to Peter Paras, Jr., whose telephone number is (571) 272-0732. The examiner can normally be reached Monday-Friday from 8:30 to 4:30 (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached at 571-272-0804. Papers related to this application may be submitted by facsimile transmission. Papers should be faxed via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Official Fax Center number is (703) 872-9306.

Inquiries of a general nature or relating to the status of the application should be directed to Dianiece Jacobs whose telephone number is (571) 272-0532.

Peter Paras, Jr.

Art Unit 1632

PETER PARAS
PATENT EXAMINER